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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,967	02/23/2004	James Oliver Dolly	17790(BOT)	6222
51957	7590	12/12/2007		
ALLERGAN, INC. 2525 DUPONT DRIVE, T2-7H IRVINE, CA 92612-1599			EXAMINER ARCHIE, NINA	
			ART UNIT	PAPER NUMBER
			1645	
			MAIL DATE	DELIVERY MODE
			12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/049,967

Applicant(s)

DOLLY ET AL.

Examiner

Nina A. Archie

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48, 50, 53-55, 57-60, 62, 69, 70, 73, 75, 104 and 105 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48, 50, 53-55, 57-60, 62, 69-70, 73, 75 is/are rejected.
- 7) ☒ Claim(s) 104 and 105 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 10, 2007 has been entered.

Amendment Entry

2. The amendment filed October 23, 2007 has been entered. Claims 48, 50, and 57-60 have been amended. Claims 49, 51-52, 56, 61, 63-68, 71-72, 74, and 76-103 have been cancelled.

Withdrawal of Rejection

3. The rejection of claims 48, 50, 53-55, 57-60, 62, 69-70, 73 and 75 under 35 U.S.C. 112, second paragraph has been withdrawn in view of applicants amendments and arguments.

4. The rejection of claims 48, 50, 53-55, 57-62, 69-70, 73 and 75 under 35 U.S.C. 102 (b) as being anticipated by Carroll et al US Patent No. 5,599,539 has been withdrawn in view of applicants amendments and arguments.

5. The rejection of claims 48, 53, 57-62, and 69 under 35 U.S.C. 102(b) as being anticipate by Roland et al 1986 CMAJ, Vol. 135 pgs. 130-131 has been withdrawn in view of applicants' amendments and arguments.

Response to Arguments

6. Applicant's arguments with respect to claims 1-3, 15, 17-19 and 40 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 48, 50, 53-55, 57-60, 62, 69-70, 73 and 75 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a vast genus of amino acid of at least 80% identity to SEQ ID NO: 42. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of amino acids of SEQ ID NO: 42, applicant must also give a functional limitation of which amino acids of SEQ ID NO:42.

The specification, however, does not disclose distinguishing and identifying features of a representative member of the genus of the amino acid of SEQ ID NO: 42 to which the claims are drawn, such as a correlation between structure of the peptide and its recited function, so that the skilled artisan could immediately envision or recognize at least a substantial number of members of the claimed genus of SNAP-25.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed'. The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally as evidenced by Greenspan et al. (Nature Biotechnology 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, Or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Therefore, absent a detailed and particular description of a

representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antigens. Therefore, in accordance with the Guidelines, the description of amino acids is not deemed representative of the genus amino acid of SEQ ID NO: 42 of the claim invention thus the claim does not meet the written description requirement.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any

inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 48, 50, 53-55, 57-60, 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Montal M. WO 97/34620.

Claims 48, 50, and 53-55 are drawn to a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25b variant having at least 80% identity to SEQ ID NO: 42 that is capable of supporting Ca^{2+} mediated exocytosis but further, capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

Montal teach a method of inhibiting the release of neurotransmitters from neuronal cells in a host comprising administering a therapeutically effective dosage of the agent (SNAP-25) to the host in lieu of a Clostridium neurotoxin to provide a therapeutic benefit to the host. Montal et al teach a SNAP 25 variant having at least 95.4% identity to SEQ ID NO: 42 (see STIC Results). Therefore Montal et al anticipate a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25b variant having at least 80% identity to SEQ ID NO: 42 that is capable of supporting Ca^{2+} mediated exocytosis but further, capable of inhibiting the

protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning. Montal teach a method, wherein a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprises a replacement of a residue at position equivalent to residue 197 of full length SNAP-25 by a residue at position 69 of SEQ ID NO: 42 (Examiner interprets "equivalent" to mean near residue 197). Therefore Montal anticipate a method, wherein a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprises a replacement of a residue equivalent to residue Q197 of SEQ ID NO: 42 by a residue other than Q; wherein residue 197 corresponds to the P1 position flanking the bond cleaved by botulinum toxin type A; a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprising a replacement comprises a replacement of a residue equivalent to residue R198 of SEQ ID NO:42 by a residue other than R; wherein residue 198 corresponds to the P1 position flanking the bond cleaved by botulinum toxin A or the P1 position flanking the bond cleaved by botulinum toxin type C1, wherein the residue equivalent to residue Q197 and R198 of SEQ ID NO: 42 is replaced by K. Montal teach that the agent (SNAP 25) is by Clostridium botulinum serotype A, E and C1. Therefore Montal anticipated the method, wherein the clostridial toxin is a botulinum toxin type A, C1, and E (see claims). Montal teach a method wherein the clostridial toxin is botulism (see abstract, claims).

9. Claims 48, 50 and 69-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montal M. WO 97/34620.

Claims 48, 50 and 69-70 are drawn to a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25b variant having at least 80% identity to SEQ ID NO: 42

that is capable of supporting Ca^{2+} mediated exocytosis but further, capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

Montal does not teach a method, wherein the patient is an infant and is an adult. However Montal teach a method of inhibiting the release of neurotransmitters from neuronal cells in a host comprising administering a therapeutically effective dosage of the agent (SNAP-25) into neuronal cells of a host in lieu of a Clostridium neurotoxin to provide a therapeutic benefit to the host. Montal et al teach a SNAP 25 variant having at least 95.4% identity to SEQ ID NO: 42.

It would have been prima facie obvious at the time the invention was made to substitute an infant and an adult as patient in a method as taught by Montal et al because Montal teach an effective dosage of SNAP 25 variant having at least 95.4% identity to SEQ ID NO: 42 into neuronal cells of a host.

Claims 48, 50, 73 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montal M. WO 97/34620 in view of Schmidt et al 1998 FEBS Letters 435 pgs. 61-64.

Claims 48, 50, 73 and 75 are drawn to a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25b variant having at least 80% identity to SEQ ID NO: 42 that is capable of supporting Ca^{2+} mediated exocytosis but further, capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

Montal is relied upon as set forth supra. However, Montal does not teach a method, further comprising a step of treating the patient with an inhibitor of the clostridial toxin. Schmidt et al teach an inhibitor of clostridial toxin, wherein the clostridial toxin inhibitor is N-acetyl-carboxamide. Schmidt et al teach that inhibitors are effective and are able to reverse or modulate toxicity (see pgs. 61-64).

It would have been prima facie obvious at the time the invention was made to incorporate a clostridial inhibitor as taught by Schmidt et al in the method of treating or preventing poisoning by a clostridial toxin in a patient in need thereof as taught by Montal because Schmidt et al teach that inhibitors are effective and are able to reverse or modulate toxicity.

Conclusion

10. No claims allowed.

Claims 48, 50, 53-55, 57-60, 62, 69-70, 73, 75, and 104-105 are rejected. Claims 104-105 are objected to as being dependent upon a rejected base claim.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is

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571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shannon Foley can be reached on 571-272-8975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Nina A Archie

Examiner

GAU 1645

REM 3B31


MARK NAVARRO
PRIMARY EXAMINER